REMARKS

Claims 1, 4-11, 14-16, 18-26, and 29-39 are currently pending in the application. Claims 1, 8-11, and 23-26 have been amended to replace the phrases "having" or "has" with "comprising" or "comprises." Claims 1 and 16 have also been amended for purposes of clarity. Accordingly, no new matter is introduced by these amendments. Accordingly, after entry of these amendments, claims 1, 4-11, 14-16, 18-26, and 29-39 will be pending in the application.

Applicant notes that a copy of the PTO Form 1449 submitted with the Information Disclosure Statement filed September 22, 2003 has been returned. However, Applicant notes that the patents and foreign patent documents listed on the PTO Form 1449 have not been initialed. Applicant respectfully requests that these citations be initialed and a new copy of the PTO Form 1449 returned to Applicant.

Applicant also notes that the Attorney Docket Number for this application has changed to HYZ-069CN (47508.530).

Applicant acknowledges that the rejections of claim 1-15 and 31-36 under 35 U.S.C. § 112, first and second paragraphs as well as under 35 U.S.C. § 103 have been withdrawn.

The outstanding rejections are addressed individually below.

1. Claims 1, 4-11, 14-16, 17-26, and 29-36 are definite.

The Office Action states that in claim 1, line 2 and claim 16, line 5 it is unclear what is meant by the term "specifically complementary." Applicant respectfully traverses this rejection. The specification defines this term at page 5, line 31 to page 6, line 13.

> The term "nucleotide sequence specifically complementary to" nucleotides 324 to 345 of a conserved *gag* region of the HIV genome is intended to mean a sequence of nucleotides that binds to the *gag* genomic RNA, proviral DNA, or

> mRNA sequence under physiological conditions, e.g., by Watson-Crick base pairing (interaction between oligonucleotide and single-stranded nucleic acid) or by Hoogsteen base pairing (interaction between oligonucleotide and double-stranded nucleic acid) or by any other means including in the case of a oligonucleotide binding to RNA, causing pseudoknot formation. Binding by Watson-Crick or Hoogsteen base pairing under physiological conditions is measured as a practical matter by observing interference with the function of the nucleic acid sequence.

Accordingly, Applicant respectfully submits that this term is definite in light of the definition in the specification. Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

The Office Action states that in claims 8-11 and 23-26, line 1, it is unclear to what the term "having" or "has" is referring . Claims 8-11 and 23-26 have been amended to replace the term "having" or "has" with "comprising" or "comprises."

Accordingly, in light of this amendment, Applicant submits that it is clear to what the term is referring. Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

2. ***Claims 1, 4-11, 14-16, 17-26, and 29-36 comply with the written description requirement.***

Claims 1, 4-11, 14-16, 17-26, and 29-36 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Applicant respectfully traverses this rejection.

The Office Action states that the specification and claims do not describe the elements that are essential to the genus comprising oligonucleotides specifically complementary to the nucleotide of SEQ ID NO:5, nor do they describe the distinguishing attributes concisely shared by the members of this broad genus. The Office Action further states, *inter alia*, that concise structural features that could distinguish structures or compounds within the genus from others are mssing from the disclosure; specific, not general guidance, is what is needed; and the disclosure fails to

provide a representative number of species to describe the genus claimed. (Office Action, pages 4-5).

M.P.E.P. §2163(II)(A)(3)(a)(ii) states that

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus . . . .
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. . . . For inventions in an unpredictable art, [Applicant submits that this art is not unpredictable] adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. . . . Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. . . . (ciations omitted)

As discussed above, the specification defines the term "specifically complementary to" at page 5, line 31 to page 6, line 13.

Thus, this definition identifies functional characteristics coupled with a known or disclosed correlation between function and structure that shows that the Applicant was in possession of the claimed invention at the time the application was filed.

In addition, the specification provides a list of representative species of oligonucleotides useful in a method of the invention in Table 2 at page 17, line 30 to page 19, line 8 of the specification. Thus, Applicant submits that a representative number of species in the genus have been described in the specification.

Furthermore, claim 1 itself recites a synthetic oligonucleotide comprising a nucleotide sequence specifically complementary to nucleotides 324 to 345 of a conserved *gag* region of the HIV-1 genome set forth as SEQ ID NO:5, the oligonucleotide consisting of 21 nucleotides, wherein the nucleotides are linked via phosphorothioate internucleotide linkages, wherein the oligonucleotide comprises at least two 5'-terminal ribonucleotides, or at least two 3'-terminal and at least two 5' terminal ribonucleotides, and wherein the ribonucleotides are 2'-substituted ribonucleotides. This case is not a situation in which the oligonucleotide is specifically complementary to an entire gene, but is complementary to a specific conserved region of that gene specified in the claims and described in the specification. Furthermore, structural modifications of this oligonucleotide are enumerated in the claim. Thus, the claim itself sets out concise structural features that could further distinguish structures or compounds within the claim from other oligonucleotides.

Accordingly, the specification and the claims provide numerous examples of representative species of the claimed genus as well as functional and structural characteristics distinguishing the claimed oligonucleotides from others. This provides specific guidance demonstrating that Applicant was in possession of the claimed invention at the time the application was filed. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

3. ***Claims 14, 15, and 34-36 are enabled.***

Claims 14, 15, and 34-36 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement over the scope claimed. Applicant respectfully traverses this rejection.

The Office Action states, *inter alia*, that the specification, while being enabling for compositions and methods of inhibiting HIV-1 infection in a cell *in vitro* or *in vivo* does not reasonably provide enablement for compositions and methods of inhibiting HIV-2 infection in a cell comprising contacting the cell with a 21 nucleobase oligonucleotide specifically complementary to SEQ ID NO:5. Applicant respectfully disagrees.

M.P.E.P § 2164.01 states that 35 U.S.C. § 112, first paragraph, "has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation." The same section further states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."

The specification does teach one of skill in the art how to *make* the invention (*see, e.g.*, the specification at page 13, line 26 to page 15, line 30 and Example 1, page 32, line 13 to page 33, line 2).

Additionally, the specification does teach one of skill in the art how to *use* the invention (*see, e.g.*, the specification at page 20, line 10 to page 21, line 30 (describing pharmaceutical formulations), page 21, line 32 to page 24, line 8 (describing therapeutically acceptable methods and amounts), page 24, lines 10-20 (describing methods of administration), and page 24, line 22 to page 26, line 24 (describing therapeutic formulations and pharmaceutical compositions)).

Therefore, the specification has fully enabled the invention as claimed because it teaches how to make and use the invention without undue experimentation.

Furthermore, the specification provides examples indicating that the invention *does* work as claimed. With regard to the enablement of compositions and methods of inhibiting HIV-2 infection, the specification indicates at page 10, lines 22-25 that FIG. 3 is "a graphic representation of the results of an XTT assay demonstrating the ability of a 4x4 oligonucleotide of the invention having SEQ ID NO:1 to inhibit HIV-2-induced cell killing." Furthermore, the specification describes at page 27, lines 31-32 that "the activity of the compounds was evaluated against HIV-2 . . . ." The results are described on page 28, lines 1-10:

> The initial experiment performed involved evaluation of Oligos 12, 32, and 41 against three laboratory strains of HIV-1 . . . and one strain of HIV-2 (ROD) in parallel with the positive control compound ddC in the XTT-based anti-HIV assay. All these olignucleotides are active against both HIV-1 and HIV-2. An enhanced level of activity was detected

> with these compounds when evaluated against the HIV-2 strain ROD. Representative results are shown in FIG. 3.

Thus, the specification does provide examples indicating that the oligonucleotides of the invention are active against HIV-2.

Furthermore, despite Applicant's previous statement indicating that the Hovanessian, *et al.* reference teaches away from the expectation that the *in vitro* inhibition of *gag* expression by antisense would lead to the *in vitro* inhibition of HIV-1 and HIV-2 replication *in vitro*, by emphasizing the differences between HIV-1 and HIV-2, rather than their similarities, Applicant has enabled compositions and methods of inhibiting HIV-2 infection. This is because the "specific sequence to which the oligonucleotides of the invention are complementary is nucleotides 324-345 of the *gag* region of HIV-1[,] . . . [which] is very conserved among strains of HIV-1, as shown . . . in TABLE 1." (Specification, page 12, lines 7-11). Thus, it is not contradictory for Hovanessian, *et al.* to teach away from the claimed invention and for Applicant to have enabled compositions and methods of inhibiting HIV-2 infection.

Accordingly, Applicant respectfully requests that this rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

In addition, Applicant notes that on page 5 of the Office Action, the Examiner has amended the Office Action to indicate that what is enabled is "directly contacting" the cell with the oligonucleotide. Applicant respectfully submits that Applicant has enabled more than "directly contacting" the cell with the oligonucleotide as described in Applicant's previous responses and as indicated by the scope of the claims for which the enablement rejection has been overcome.

CONCLUSIONS

In view of the arguments set forth above, Applicant respectfully requests reconsideration and reexamination of the above-referenced patent application. Applicant submits that the rejections contained in the Office Action mailed on December 19, 2003, have been overcome, and that the claims are in condition for allowance.

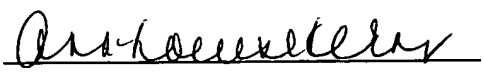
Applicant encloses herewith a Petition for a One-Month Extension of Time up to and including April 19, 2004, to respond to the Office Action mailed December 19, 2003. Please charge our Deposit Account No. 08-0219 the $55.00 fee for this purpose.

Applicant also encloses herewith an Information Disclosure Statement. Please charge our Deposit Account No. 08-0219 the $180.00 fee for this purpose.

No other fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

If the Examiner believes that any further discussion of this communication would be helpful, please contact the undersigned at the telephone number provided below.

Respectfully submitted,



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